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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| ANDRES, JANET L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | |

DATE MAILED: 04/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/662,756 | ECONOMIDES ET AL. | |
| | Examiner | Art Unit | |
| | Janet L. Andres | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-13 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) 8 is/are allowed.

6)☒ Claim(s) 1,3-7 and 9-13 is/are rejected.

7)☒ Claim(s) 2 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 1-13 are pending and under examination in this office action.

### *Specification*

2. The disclosure is objected to because of the following informalities: Application 09/762960 has issued as U.S. patent 6,660,499. The first line of the specification should be updated accordingly.

### *Claim Rejections - 35 USC § 101*

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claim 4 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim does not require that the antibody be isolated and thus encompasses products of nature, which are non-statutory.

### *Claim Rejections - 35 USC § 102*

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1 and 3 are rejected under 35 U.S.C. 102(a) as being anticipated by Saegusa et al., June, 1998, Dev. Growth and Differentiation, vol. 40(3), pp. 343-353.

Saegusa et al. teaches mouse PRDC, the polynucleotide sequence of which is 87.7% identical to instant SEQ ID NO: 11 (Fig. 4, p. 349). According to Applicant's own teachings, the

encoded proteins are 95% identical (p. 11). While means of protein expression are not explicitly taught, a person of ordinary skill would envisage such expression from the disclosed sequence and further from the teachings on p. 352, column 2, that expression of the protein is desirable. If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. See In re Petering, 133 USPQ 275 (CCPA 1962). The polypeptide was therefore in the public domain, although it was not explicitly disclosed. While claim 1 contains no structural limitations, the term "DCR5" as it is described in the specification does not limit the protein to a single sequence; see p. 2, paragraph 10. PRDC would also be expected to have the same biological activity of the protein of SEQ ID NO: 12, meeting the limitations of claim 3.

It is noted that claim 1 contains the limitation that the polypeptide must be human, while PRDC was derived from mouse. However, the origin of a sequence is not reflected in any aspect of its structure or function; once isolated, the nature of the animal from which is was derived cannot be determined. Thus the qualification that the sequence be human is not given patentable weight; the source the molecule does not impart any characteristics that would distinguish it from other molecules encompassed by the structural limitations of the claims.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 4-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saegusa et al. in view of Harlow and Lane, Antibodies, 1989.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Saegusa et al. teaches as set forth above but fails to teach the antibodies of claims 4, 5, and 7 or the pharmaceutically acceptable compositions of claim 6. Harlow and Lane teach antibodies, means of producing them, and techniques using them throughout (see, for example, pp. 361, 473, and 555), and particularly teach uses for monoclonal antibodies on p. 142. Many of these techniques require that the antibody and protein be in a pharmaceutically acceptable carrier. It would have been obvious to one of ordinary skill in the art to combine the teachings of Saegusa et al. with those of Harlow and Lane to produce antibodies, in particular monoclonal antibodies, and to place such antibodies as well as the proteins to which they bind in a pharmaceutically acceptable carrier. One of ordinary skill would have been motivated to do so because Saegusa et al. provides a protein of biological interest in neuronal development and Harlow and Lane teach antibodies as tools for exploring protein function and methods for using them. Thus one of ordinary skill would have expected such antibodies and methods to be useful for research into the role of the protein identified.

9. Claims 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saegusa et al. in view of Ashkenazi et al. (Current Opinion in Immunology, 1997, vol. 9, pp. 195-200).

Saegusa et al. teaches as set forth above but fails to teach the fusion proteins of claims 10 and 11. Ashkenazi et al. teaches that such proteins are useful for various purposes, including research studies to dissect molecular interactions as well as other functional and structural studies (p. 198, column 1). It would have been obvious to one of ordinary skill in the art to combine the teachings of Saegusa et al. with those of Ashkenazi et al. to produce fusion proteins. One of ordinary skill would have been motivated to do so because Saegusa et al. provides a protein of biological interest in neuronal development and Ashkenazi et al. teaches fusion proteins as tools for exploring protein function and methods for using them. Thus one of ordinary skill would have expected such fusion proteins to be useful for research into the role of the protein identified.

***Claim Rejections - 35 USC § 112***

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses one isolated protein sequence. Claim 3, however, is drawn to sequences comprising fragments of the disclosed sequence. Thus, it encompasses sequences that

can vary substantially in length and in composition from the disclosed sequence. There is no description of the required structural and functional features of the claimed molecules, or of the conserved regions that would be critical for these features. Since these features are not disclosed, there is no way to determine what variations could be tolerated without altering them, or what sequences comprising fragments would possess the same defining characteristics. Further, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polynucleotides encompassed; Saegusa et al. teaches no structural or functional features by which polypeptides with the same characteristics could be identified. Therefore, applicant has not disclosed sufficient species or common structural features such that one skilled in the art would conclude that applicant was in possession of the claimed genus of sequences comprising fragments of DCR-5 proteins.

12. Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman,* (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands,* 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

These claims are drawn to methods of regulating cartilage and bone growth with either the DCR5 protein or an antibody. While Applicant has shown that the protein can bind to BMP-2 and BMP-4, there is no guidance to indicate that this binding, or inhibition of it, could be used to affect any conditions *in vivo*. No conditions are described in which the protein could be used to affect BMP activity with a resulting effect on bone or cartilage, and no conditions are described in which the protein itself could be usefully inhibited with a resulting effect on bone or cartilage. The prior art fails to provide compensatory guidance; what is taught for the closely related PRDC protein is a role in neuronal function. Thus without further guidance as to what conditions the protein, or an antibody against it, could be used to treat, it would require undue experimentation to practice the invention as claimed.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1, 3-7, and 9-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite in the recitation of "DCR-specific activity". While Applicant discloses binding to BMP-2 and BMP-4 in example 3, there is no definition of "DCR-specific activity". One of skill in the art would not know what activities were encompassed, and thus what polypeptides would meet the limitations of the claims.

Claims 4 and 5 are drawn to antibodies that specifically bind DCR5. Applicant has provided no definition of what degree or quality would be specific; thus one of skill in the art would be unable to determine what binding would be considered to be specific.

As written, claim 9 lacks antecedent basis for "the protein" as well as "the host cell". It appears that Applicant intended the claim to depend from claim 8 and for purposes of examination it has been interpreted as so depending.

Claims 1, 3-7, and 10-13 are drawn to polypeptides identified as "human DCR5", antibodies against them, and means of using the polypeptides and antibodies. The use of the term "DCR5" is indefinite because it only describes the protein of interest by an arbitrary name. Applicant's specification does not serve to limit DCR5 to any particular polypeptide or set of polypeptides; while the polypeptide of SEQ ID NO: 12 and related molecules are clearly encompassed by the direction on pp. 1-3, there is no definition of DCR5 by which one of skill in the art would be able to ascertain the definitive characteristics of DCR5 and thus determine which molecules are encompassed and which are not.

***Allowable Subject Matter***

Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

CLAIMS 1, 3-7, AND 9-13 ARE REJECTED. CLAIM 2 IS OBJECTED TO. CLAIM 8 ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Andres whose telephone number is 571-272-0867. The examiner can normally be reached on Monday-Thursday and every other Friday, 8:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Andres, Ph.D.
27 April 2004